application serial number 08/934,367. A provisional terminal disclaimer is filed herewith.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 11, 12, 14 and 15 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Specifically, the Examiner has contended that Table 1, at page 40 of the instant specification renders claims 11, 12, 14 and 15 inoperative.

35 U.S.C.§ 112, first paragraph states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In the instant application, claims 11, 12, 14 and 15 are directed to a method of increasing the concentration of HDL in the blood of a mammal by:

"(a) immunizing said mammal with an inoculum containing a vehicle in which is dissolved or dispersed a CETP immunogen that is a fusion protein of

(i) an exogenous antigenic carrier polypeptide..." and

"(c) repeating said immunizing step until the HDL cholesterol value in the blood of said mammal is increased to about 10 percent relative to the HDL cholesterol value prior to said first immunization step."

A careful reading of the specification reveals that Example 2 (p. 38-40), and in particular Table 1, only represents antibodies and HDL values for the first-immune sera (*not* the boosted sera). Thus, Table 1 represents a comparison of pre-immune sera and

first-immune sera. Table 1 illustrates that even after a single inoculation, a measurable increase occurs in HDL levels.

The procedure for Example 2 is specified on pages 38-40:

> "This study utilized 30 New Zealand white rabbits in three groups with 10 rabbits per group. Three immunogens were utilized in this study: (1) Recombinant human CETP, (2) the carboxy-terminal 26 amino acid residues of rabbit CETP (SEQ ID NO:50), and (3) a control immunogen whose amino acid residue sequence was unrelated to that of CETP.
>
> Pre-immune sera were collected before immunization with the respective immunogens. The purpose of this study was to illustrate that the above CETP immunogens would induce anti-CETP-specific (autogeneic anti-CETP) antibodies in rabbits, and that the autogeneic antibodies generated against CETP bind to (immunoreact with) the endogenous rabbit CETP, and thus lessen the transfer of cholesteryl esters from HDL particles and raise the level of HDL in the hosts.
>
> The above immunogens were emulsified in CFA. Each rabbit received 500 μg of one of the immunogens emulsified in CFA immunized by sub-cutaneous route. Seven weeks later *the first bleed post-immune sera were collected.*
>
> ***
>
> The results of this study on the elevation of HDL particle concentration in the blood (plasma) of the host mammals (mean ±.S.D.) are shown in Table 1, below, *for those first-immune sera.*" (emphasis added).

In contrast, Example 1 (p.35-38) describes immunizing rabbits with multiple inoculations of immunogen.

However, the claims at issue require "repeating said immunization step until the HDL cholesterol value in the blood of said mammal is increased by about 10 percent..." While Example 2 states that more immunizations were later performed, Table 1 does not represent those data. Therefore, the claims in question, 11, 12, 14 and 15, are not merely enabled by Table 1 in isolation, but rather are enabled by *all* of the examples.

It is thus respectfully asserted that the rejection under 35 U.S.C. § 112, first paragraph is improper. The PTO cannot make this [lack of enablement] rejection unless it has reason to doubt the objective truth of the statements contained in the written description. See In re Brana, 51 F.3d 1560,1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."); see also In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) ("[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."). The PTO may establish a reason to doubt an invention's asserted utility when the written description "suggest[s] an inherently unbelievable undertaking or involve[s] implausible scientific principles." Brana, 51 F.3d at 1566, 34 USPQ2d at 1441; see also In re Eltgroth, 419 F.2d 918, 164 USPQ 221 (CCPA 1970) (control of aging process).

In the instant application, there is ample enabling disclosure of the method of claim 11, including the procedure for Example 2 on pages 38-40.

Furthermore, the Examiner has not presented evidence to refute the enablement of repeatedly immunizing a mammal with an inoculum containing a vehicle in which is

dissolved or dispersed a CETP immunogen until the HDL cholesterol value in the blood of said mammal is increased to about 10 percent relative to the HDL cholesterol value prior to a first immunization.

It is therefore respectfully requested that the rejection under 35 U.S.C. § 112, first paragraph be removed, and the case be passed to issue.

Respectfully submitted,

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